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12 *Attorneys for Plaintiffs The Regents of the University of Michigan and*
13 *The University of South Florida Board of Trustees*

**UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF CALIFORNIA
SAN JOSE DIVISION**

16 THE REGENTS OF THE UNIVERSITY OF
17 MICHIGAN,
18 and
THE UNIVERSITY OF SOUTH FLORIDA
BOARD OF TRUSTEES.

Case No.

COMPLAINT FOR PATENT INFRINGEMENT

Plaintiffs

JURY TRIAL DEMANDED

21 | Page

22 NOVARTIS PHARMACEUTICALS CORPORATION

24 | Defendant.

1 This is a civil action for patent infringement of United States Patent No. 10,633,344 (“the
2 ’344 patent”) under the patent laws of the United States, 35 U.S.C. § 271, *et seq.* Plaintiffs, which
3 are the corporate entities of two academic institutions, invested in groundbreaking advances in the
4 fields of chemical engineering and pharmaceutical sciences. As part of Plaintiffs’ investment in
5 and support of innovative and collaborative research, the named inventors of the ’344 patent—
6 Drs. Michael Zaworotko, Brian Moulton, and Nair Rodríguez-Hornedo—devoted their individual
7 expertise in supramolecular technology and pharmaceutical sciences to develop improved
8 pharmaceutical compounds. Through the inventors’ collaboration, the ’344 patent issued. The
9 ’344 patent relates to pharmaceutical compositions comprising, among other things,
10 therapeutically effective amounts of a co-crystal comprising supramolecular synthons with the
11 claimed elements. Without obtaining a license or permission to use the inventions claimed in the
12 ’344 patent, Novartis makes, uses, tests, sells, offers for sale and/or imports its co-crystal drug
13 Entresto®, which directly infringes, literally and/or under the doctrine equivalents, one or more
14 claims of the ’344 patent.

15 Accordingly, Plaintiffs The Regents of the University of Michigan and The University of
16 South Florida Board of Trustees (collectively, “Plaintiffs”) file this Complaint and demand for a
17 jury trial seeking relief for patent infringement by Novartis Pharmaceuticals Corporation
18 (“Novartis” or “Defendant”). Plaintiffs state and allege the following:

THE PARTIES

20 1. Plaintiff The Regents of the University of Michigan is a constitutional corporation
21 of the State of Michigan, having a principal address at Ruthven Building 2300, 1109 Geddes
22 Avenue, Ann Arbor, Michigan 48109-1079.

2. Plaintiff The University of South Florida Board of Trustees is the public body
corporate of the University of South Florida, an academic institution organized and existing under
the laws of the State of Florida, with its principal place of business located at 4202 E. Fowler
Avenue, Tampa, Florida 33620.

3. On information and belief, Defendant Novartis Pharmaceuticals Corporation is a corporation organized and existing under the laws of the State of Delaware, with its principal place of business in 1 Health Plaza, East Hanover, New Jersey 07936-1080.

JURISDICTION

4. This is a civil action for patent infringement under the patent laws of the United States, 35 U.S.C. § 271, *et seq.* This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1338.

5. This Court has personal jurisdiction over Novartis pursuant to the laws of the State of California, including California Code of Civil Procedure § 410.10, because Novartis is engaged in substantial and not isolated activity at its regular and established place of business within this judicial District. This Court has specific jurisdiction over Novartis because Novartis (a) has committed acts of infringement in this District giving rise to this action; and (b) has established more than minimum contacts within this judicial District, such that the exercise of jurisdiction over Novartis in this Court would not offend traditional notions of fair play and substantial justice.

6. Novartis has admitted that this Court has personal jurisdiction over Novartis and has admitted that Novartis regularly and continuously transacts business in this jurisdiction. See *Plexxikon Inc. v. Novartis Pharmaceuticals Corporation*, No. 4:17-CV-04405-HSG, Dkt. No. 61 (Amended Answer) at 2-3, (N.D. Cal. Jan. 25, 2018). Novartis has further admitted that it derives substantial revenue from the sale of drug products in the State of California. See id. Lastly, Novartis has admitted that it maintains and operates facilities in this District at least at 150 Industrial Road, San Carlos, California 94070. See id.

7. On information and belief, Novartis has systematic and continuous contacts with this judicial District and regularly and continuously conducts business in California, including by selling drugs products in California.

8. On information and belief, Novartis is a large pharmaceutical company that is engaged in the business of marketing, distributing, promoting, testing, labelling, and selling the drug Entresto®.

9. On information and belief, Novartis is the holder of the New Drug Application (NDA) No. 207620 by which the Food & Drug Administration (FDA) granted approval in July 2015 for the commercial manufacturing, marketing, sale, and use of Entresto® (sacubitril and valsartan) tablets.

10. On information and belief, Novartis markets and distributes Entresto® throughout the world, including all fifty states in the United States, and throughout California, and has established distribution channels for drug products in California.

11. On information and belief, Novartis maintains a campus in Emeryville, California at 5959 Horton Street, Emeryville, California 94608. On information and belief, Novartis' Emeryville campus is focused on research and development and employs 50 employees, including research professionals.

12. Additionally, Novartis has purposefully availed itself of the benefits and protections of this state, *inter alia*, by filing a complaint for patent infringement in this judicial District. See *Novartis Pharmaceuticals Corp. v. Handa Neuroscience, LLC*, 3:21-CV-03397, Dkt. No. 7 (Complaint), (N.D. Cal. May 6, 2021).

13. Venue is proper over Novartis in this judicial District pursuant to 28 U.S.C. § 1400(b) because Novartis maintains a regular and established place of business at its San Carlos and Emeryville campuses, and because it has committed acts of patent infringement within this judicial District.

THE ASSERTED PATENT

14. On April 28, 2020, United States Patent No. 10,633,344 (“the ’344 patent”) entitled “Multiple-Component Solid Phases Containing at least One Active Pharmaceutical Ingredient” was duly and legally issued by the United States Patent and Trademark Office. A true and correct copy of the ’344 patent is attached as **Exhibit A**.

15. The '344 patent is a continuation of United States Patent Application No. 10/378,956, filed on March 3, 2003, which claims priority to a provisional application filed on March 1, 2002.

16. Drs. Michael Zaworotko, Brian Moulton, and Nair Rodríguez-Hornedo are the named inventors of the '344 patent. Drs. Zaworotko and Moulton assigned their rights as inventors of the '344 patent to The University of South Florida Board of Trustees, and Dr. Rodríguez-Hornedo assigned her rights as an inventor of the '344 patent to the Regents of the University of Michigan. Plaintiffs are currently the owners of the entire right, title, and interest of the '344 patent.

BACKGROUND

17. This case is brought by the corporate entities of two academic institutions that invest in groundbreaking advances in the field of chemical engineering and pharmaceutical sciences, among many other fields. Both the University of Michigan and the University of South Florida are nationally recognized as top public research institutions.

18. The University of Michigan is one of the largest and most diverse research universities in the world, and plays a significant role both in generating a steady stream of innovative ideas and in educating the people who together underlie the nation's economic success and quality of life. The University of Michigan is internationally recognized as a top-tier research institution, last publicly reporting about \$1.58 billion in annual research expenditures. The University of Michigan invests substantial resources into research and development activities,

1 which is reflected by its extensive patent portfolio covering a wide range of technologies in many
2 disciplines, including chemical engineering and pharmaceutical sciences.

3 19. The University of South Florida is a major research institution designated as a
4 Preeminent State Research University by the Florida Board of Governors and recognized as a top
5 public research university. In 2019, the University of South Florida was awarded \$525.4 million
6 in research grants, putting it at the forefront of research in medicine, science, engineering, the arts,
7 and more.

8 20. As a result of Plaintiffs' investment in and support of innovative and collaborative
9 research, the named inventors of the '344 patent—Drs. Michael Zaworotko, Brian Moulton, and
10 Nair Rodríguez-Hornedo—devoted their individual expertise in supramolecular technology and
11 pharmaceutical sciences to develop improved pharmaceutical compounds.

12 21. Dr. Michael Zaworotko received his Bachelor's in Science from Imperial College
13 in 1977 and a doctorate degree from the University of Alabama in 1982. Dr. Zaworotko was a
14 professor in the chemistry department at the University of South Florida from 1999 to 2013 during
15 the collaborative work that led to the '344 patent. In 2013, Dr. Zaworotko joined the faculty at the
16 University of Limerick, Ireland.

17 22. Dr. Brian Moulton received his doctorate degree in chemistry from the University
18 of South Florida in 2003. During his time at the University of South Florida, Dr. Moulton worked
19 with Dr. Zaworotko, co-authoring several publications related to co-crystal engineering.

20 23. Dr. Nair Rodríguez-Hornedo received a bachelor's degree in pharmacy from the
21 University of Puerto Rico in 1975, and master (1977) and doctorate (1984) degrees in
22 pharmaceutical sciences from the University of Wisconsin-Madison. Dr. Rodríguez-Hornedo was
23 a research scientist in the pharmaceutical industry in 1984-1985, and assistant professor at the
24 University of Arizona in 1985, before joining the faculty at the University of Michigan in 1989.
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Dr. Rodríguez-Hornedo was an associate professor in 1994 and professor in 2016. She was named professor emerita of pharmaceutical sciences at the University of Michigan in 2022.

24. The inventions disclosed in the '344 patent were a result of the collaborative research performed by Drs. Zaworotko, Moulton, and Rodríguez-Hornedo with the support of the University of Michigan and the University of South Florida. The '344 patent recognizes the unmet goal of predictable crystal structure from crystal engineering, *see Ex. A* at 1:33-35, and the patented invention applies the concepts of crystal engineering to design new pharmaceutical compounds, *id.* at 3:29-34. In particular, the '344 patent relates to “multiple-component solids having at least one active pharmaceutical ingredient” to achieve crystalline assemblies with “improved drug solubility, dissolution rate, stability and bioavailability.” *Id.* at 3:12-28.

COUNT I
Infringement of the '344 Patent Under 35 U.S.C. § 271(a)

25. Plaintiffs restate and reallege the preceding paragraphs of this Complaint.

26. Novartis has directly infringed, and continues to directly infringe, literally and/or under the doctrine of equivalents, one or more claims of the '344 patent by making, using, testing, selling, offering for sale and/or importing into the United States the Accused Products under 35 U.S.C. § 271(a). The Accused Products include the Entresto® tablets at various dose strengths: low strength (24.3 mg sacubitril, 25.7 mg valsartan); middle strength (48.6 mg sacubitril, 51.4 mg valsartan); and/or high strength (97.2 mg sacubitril, 102.8 mg valsartan).

27. The Accused Products practice all of the elements of at least exemplary claim 10 of the '344 patent.

28. Each dosage strength of Entresto® is a pharmaceutical composition indicated to reduce the risk of cardiovascular death and hospitalization for heart failure in adult patients with chronic heart failure, and for the treatment of symptomatic heart failure with systemic left

ventricular systolic dysfunction in pediatric patients aged one year and older. See **Exhibit B**, Entresto® Drug Label.

29. Each dosage strength of Entresto® comprises a pharmaceutically acceptable carrier. For example, Entresto® is a tablet comprising microcrystalline cellulose and other inactive ingredients. *See id.* at 14.

30. Each dosage strength of Entresto® comprises a therapeutically effective amount of a co-crystal comprising supramolecular synthons, containing sacubitril-valsartan co-crystals comprising supramolecular synthons. *See Exhibit C* at 1, “LCZ696: A Dual-Action Sodium Supramolecular Complex,” Tetrahedron Letters, 53 (2012) 275-76.

31. Each supramolecular synthon is formed from stoichiometric amounts of at least one active pharmaceutical ingredient, for example sacubitril, and one co-former, for example valsartan. **Exhibit B** at 13.

32. As one example, an active pharmaceutical ingredient, sacubitril, has a first chemical functionality, a carboxamide, that permits formation of API homosynthons through non-covalent hydrogen bonding when sacubitril is in its pure form. **Exhibit C** at 1.

33. As one example, a co-former, valsartan, has a second chemical functionality, a tetrazole, that is complimentary to sacubitril's first chemical functionality, a carboxamide, via non-covalent hydrogen bonding. See **Exhibit C** at 1.

34. As one example, the co-former, valsartan, is a solid at room temperature and atmospheric pressure when valsartan is in its pure form.

35. Supramolecular synthons are formed between, as one example, the first chemical functionality of sacubitril, a carboxamide, and the second chemical functionality of valsartan, a tetrazole, via non-covalent hydrogen bonding. *See Exhibit C* at 1.

PRAYER FOR RELIEF

1 WHEREFORE, Plaintiffs The Regents of the University of Michigan and The University of
2 South Florida Board of Trustees respectfully request that this Court:

- 3 1) Enter judgment that Novartis has infringed one or more claims of the Asserted Patent;
4 2) Award Plaintiffs damages in an amount sufficient to compensate it for Novartis'
5 infringement of one or more claims of the Asserted Patent, together with pre-judgment and
6 post-judgment interest costs, and all other damages permitted under 35 U.S.C. § 284;
7 3) Declare that this be an exceptional case within the meaning of 35 U.S.C. § 285;
8 4) Award Plaintiffs their costs in this action, together with reasonable attorneys' fees and pre-
9 judgment and post-judgment interest;
10 5) Perform an accounting of Novartis' infringing activities through trial and judgment;
11 6) Award Plaintiffs such other and further relief, including other monetary and equitable
12 relief, as this Court deems just and proper.

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DEMAND FOR JURY TRIAL

17 Pursuant to Federal Rule of Civil Procedure 38(b), Plaintiffs demand a jury trial on all issues
18 so triable.
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20 Dated: August 29, 2022

Respectfully Submitted,

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